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Comparison of ketamine and magnesium sulphate for the prevention of postoperative shivering in gynaecological surgery: A randomized, prospective, placebo-controlled study

Ketamine vs. Magnesium sulphate for shivering

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Abstract

Aim: Post-anaesthesia shivering is a common complication that reduces patient comfort and increases morbidity and mortality risks due to physiological stress. This study aimed to compare the effects of ketamine and MgSO4 on postoperative shivering, pain, and recovery after gynecological surgeries.

Material and Methods: In this randomized, prospective, placebo-controlled study, 60 patients (ASA I-II, aged 18-65 years) undergoing elective gynecological surgery were divided into magnesium sulfate (n = 20), ketamine (n = 20), and placebo (n = 20) groups. Heart rate, mean arterial pressure, tympanic membrane temperature, shivering scores, Aldrete recovery scores, and Visual Analog Scale (VAS) values were recorded at T1-T10 time points to evaluate drug efficacy.

Results: Magnesium and ketamine showed similar efficacy in preventing shivering, both being superior to placebo. A significant decrease in systolic and diastolic arterial pressure was observed in the magnesium group during recovery. VAS scores were significantly higher in the placebo group. Tympanic membrane temperatures decreased in the ketamine group, and all placebo group patients undergoing laparoscopic surgery experienced shivering.

Discussion: Subanaesthetic doses of ketamine and low-dose magnesium had comparable effects on shivering, hemodynamics, and recovery in gynecological surgeries under general anesthesia, and both reduced postoperative VAS scores compared to placebo.

Keywords

Postoperative Shivering, Magnesium Sulphate, Ketamine, Gynaecological Surgery

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Introduction

Post-anesthesia tremor is a common complication after general and regional anesthesia. The incidence of this condition, which occurs in 5-65% of patients after general anesthesia and 33% after regional anesthesia, varies depending on the type of anesthesia used, the age and sex of the patient, and the length of the surgical period [1].

The prevention and treatment of shivering after anesthesia are critically important for both patient safety and the quality of care. Shivering can seriously reduce patient comfort and lead to a range of negative outcomes, including a 100-600% increase in oxygen consumption, elevated carbon dioxide production, tachycardia, hypertension, delayed wound healing, and an increased risk of postoperative morbidity and mortality. It is known that these complications prolong the postoperative recovery process and reduce patient satisfaction [2].

The treatment of post-anesthesia shivering includes pharmacological approaches, involving various agents from biogenic amines to NMDA receptor antagonists [3]. Among these agents, magnesium sulfate (MgSO4) and ketamine stand out due to their capacities to modulate central thermoregulatory control mechanisms. Magnesium, while taking on many important roles in physiological systems, is thought to exert its analgesic effect through calcium channel blockade and NMDA receptor antagonist properties [4]. Ketamine, as a non-competitive NMDA receptor antagonist, offers an effective option for reducing postoperative pain and preventing shivering [5].

Literature reviews indicate that there are limited studies comparing the effects of MgSO4 and ketamine on postoperative shivering. In this study, we aimed to provide information about the efficacy of these two agents by comparing the effects of ketamine and MgSO4, administered in specific doses after gynecological surgeries, on postoperative shivering, pain, and recovery.

Material and Methods

Our study was conducted prospectively as a placebo-controlled, double-blind trial. A total of 60 patients, aged 18-65, ASA I-II risk class, undergoing elective gynecological surgery under general anesthesia were included.

Exclusion criteria included patients with surgery durations shorter than 1 hour or longer than 3 hours, those with a body mass index (BMI) >35 kg/m^2, allergies to induction agents, severe cardiovascular or pulmonary diseases, and renal or hepatic failure. New patients were included to replace any excluded individuals.

One day before surgery, all patients underwent pre-anesthetic evaluation and written informed consent was obtained. During anesthesia, non-invasive monitoring of blood pressure (MAP), heart rate (HR), oxygen saturation (SpO2), and ECG was performed. An 18G IV catheter was placed, and a 0.9% NaCl infusion was started. Tympanic membrane temperature was measured to assess core body temperature.

After standard anesthesia induction, patients were intubated and connected to a mechanical ventilator. During fascia closure, one of three randomly assigned solutions was administered: Group M received 30 mg/kg magnesium sulfate, Group K received 0.5 mg/kg ketamine hydrochloride, and Group P received a 15 mL saline bolus. After anesthesia cessation, when spontaneous respiration was restored, patients were extubated and transferred to the recovery room.

The patients' tympanic body temperature, Pulse oximeter, mean arterial blood pressure, as well as peripheral oxygen saturation, were measured before induction (T1), after intubation (T2), at the 30th minute of surgery (T3), and before drug administration (T4); extubation, surgery, and anesthesia durations were recorded. Postoperative measurements and recordings were made by an anesthetist who was unaware of the intraoperatively administered medication. Spontaneous eye opening, response to verbal stimuli, entry into the recovery room (T5), and at 10 (T6), 20 (T7), 30 (T8), 45 (T9), and 60 (T10) minutes, hemodynamic parameters, tympanic membrane temperatures, room temperature, and additional drug injections (meperidine, sodium diclofenac, metoclopramide) were recorded. The patients' shivering scores, Aldrete recovery scores, anxiety scores, and pain scores (VAS) were calculated. When the Aldrete score was 8 or above, agitation scores were evaluated.

Statistical analysis

The data were analyzed using SPSS 11.5. Normal distribution was evaluated using the Kolmogorov-Smirnov test. Parametric data (age, BMI, hemodynamics, etc.) were analyzed using ANOVA, ordinal data with the X^2 test, and nonparametric data with the Kruskal-Wallis Variance Analysis. Within-group parametric evaluations were conducted using Repeated Measures ANOVA. Parametric data were presented as mean ± standard deviation, while nonparametric data were presented as percentages or counts. The significance level was set at <0.05.

Power analysis

In this study, power analysis was performed to increase statistical power and determine the appropriate sample size. In determining the sample size, a similar study, by Kose et al. (4) (2008), was taken as a reference.

Power analysis was performed based on the significance level ($\alpha = 0.05$) and 80% power ($1-\beta = 0.80$) criteria. Considering the sample size in the study of Köse et al., the minimum sample size required to observe a similar effect was calculated. The analysis was performed using G*Power 3.1 software, and power calculations were performed according to the relevant test type (e.g. independent sample t-test, ANOVA, regression analysis, etc.).

As a result, it was determined that the sample size used in our study provided sufficient statistical power. Thus, the reliability and generalizability of the findings were increased.

Ethical Approval

This study was approved by the Ethics Committee of Karadeniz Technical University (Date: 2010-01-08, No:588).

Results

This study was conducted on 60 patients after obtaining approval from the local ethics committee and patient consent. The patients' ages, BMI (Body Mass Index), ASA scores, anesthesia, and surgical durations among the groups are shown in Table 1; there was no statistically significant difference between the groups ($p > 0.05$) (Table 1).

Table 1. Patients' General Characteristics and Intraoperative Data

	Group M (n=20)	Group K (n=20)	Group P (n=20)
Age	45,05 ± 7,53	47,80 ± 6,35	43,45 ± 6,78
ASA (I/II)	8.12	9.11	12.8
BMI (kg/m2)	26,99 ± 2,72	27,35 ± 2,37	25,64 ± 2,64
Operation time (min)	84,75 ± 23,08	102,75 ± 29,4	96,75 ± 32,29
Anesthesia time (min)	97,75 ± 24,94	118,75 ± 29,01	109,25 ± 34,2

Data of patients are expressed as numbers, mean ± standard deviation. BMI; body mass index. ASA; American Society of Anesthesiologists

Table 2. Tremor Score Measurements of Three Groups

	Group M (n=20)	Group K (n=20)	Group P (n=20)
T5	0(0-3)	0(0-3)	0(0-4)
T6	0(0-1)	0(0-2)	1.5(0-4) *
T7	0(0-3)	0(0-2)	0(0-4)
T8	0(0-4)	0(0-2)	0(0-3)
T9	0(0-1)	0(0-4)	0(0-3)
T10	0(0-1)	0(0-2)	0(0-2)

* p < 0.05: Tremor score measurement is statistically significantly higher in T6 Group P compared to other groups.

Table 3. Postoperative Visual Analogue Scale (VAS) of the Groups

	Group M (n=20)	Group K (n=20)	Group P (n=20)
T5	0 (0-3)	0(0-4)	0(0-5)
T6	0,5 (0-5)	0(0-6)	2(0-6) *
T7	1.5(0-6)	1(0-6)	3(0-6) *
T8	2(0-4)	1,5(0-6)	2(1-6)
T9	2(0-4)	2.5(0-6)	2(1-4)
T10	2(0-4)	2(0-4)	2(0-4)

* p < 0.05, There was a statistically significant increase in Sedation Agitation Score at T6 and T7 in Group P compared to the other two groups.

The heart rates (beats/min) of the patients included in the study were evaluated over all time points (T1-T10) according to the groups. There was no statistically significant difference between the groups in terms of heart rates (p > 0.05) (Figure 1). The changes in the Mean Arterial Pressure (MAP) values (mmHg) of the cases included in the study over all time points (T1-T10) according to the groups. No statistically significant difference was observed between the groups in terms of OKB values (p > 0.05) (Figure 2).

In terms of body temperature measurement values between the groups; at the 30th minute of the recovery period (T8), there was a statistically significant decrease in Group K compared to Group P. Additionally, at the 45th minute (T9), there was a statistically significant decrease in Group K compared to Group P (p < 0.05). Finally, at the 60th minute (T10), there was a statistically significant decrease in Group K compared to Group P (p < 0.05) (Figure 3).

Between the groups, in terms of the measurement values of the Tremor score during the collection period at the 10th minute (T6), there was a statistically significant increase in Group P compared to the other two groups (p < 0.05) (Table 2).

When the patients were examined in terms of postoperative visual acuity scale (VAS) values, a statistically significant higher

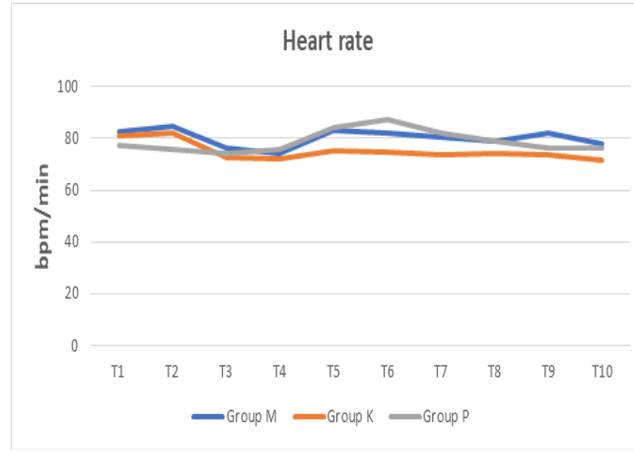

Figure 1. Trend of heart rate in three groups

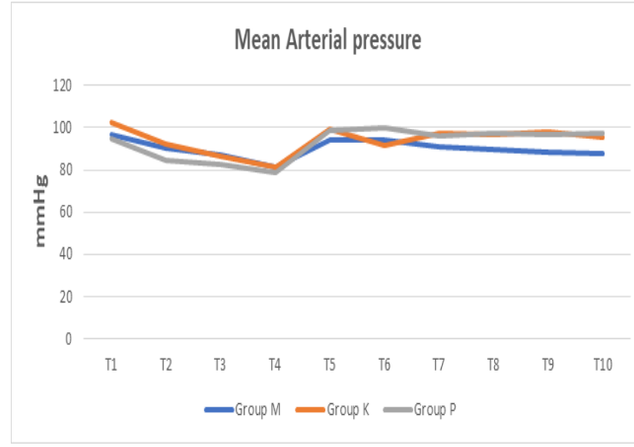

Figure 2. Trend of mean arterial pressure in three groups

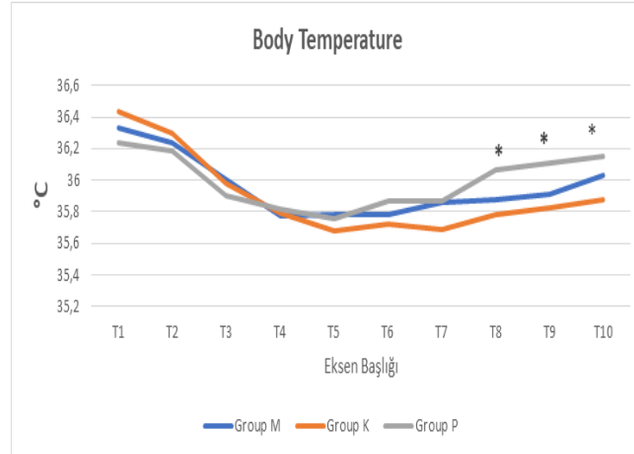

Figure 3. Trend of body temperature in three groups

value was found in Group P compared to the other groups at the 10th minute (T6) and 20th minute (T7) of the recovery period. (p < 0,05) (Table 3).

Discussion

This study demonstrates that magnesium sulfate ($MgSO_4$) and ketamine are effective options for managing postoperative shivering by influencing thermoregulation. Based on the anesthesia methods, drug applications, and hemodynamic stability observed in our study, these treatment options appear to be both safe and effective.

The literature indicates that men are more prone to shivering

after anesthesia, while age can impair thermoregulatory control [6]. A higher BMI has been associated with a lower incidence of shivering [7]. In our study, since all participants were women and BMI levels were similar across groups, these factors were not considered in the analysis.

Previous studies have found a correlation between anesthesia duration and shivering, with longer procedures increasing the likelihood of shivering [6, 8]. In our study, surgeries lasting less than 60 minutes or more than 180 minutes were excluded to maintain a consistent anesthesia duration range. Our findings align with existing literature, supporting the relationship between prolonged anesthesia and increased shivering incidence.

The choice of anesthesia significantly affects shivering occurrence. Certain agents, such as halothane, isoflurane, fentanyl, and nitrous oxide, lower the thermoregulatory vasoconstriction threshold [9]. Chang et al. found that propofol-nitrous oxide anesthesia resulted in a lower incidence of postoperative shivering compared to thiopental-isoflurane-nitrous oxide anesthesia [10]. In our study, thiopental and sevoflurane were standardized for all patients. While opioids like fentanyl can influence thermoregulation and reduce shivering [11], no significant difference in shivering rates was observed with fentanyl use in our study, despite literature suggesting a potential effect [12].

$MgSO_4$'s cardiovascular effects are primarily due to its vasodilatory properties, which relax vascular smooth muscles [12]. Mendonca et al. reported an increase in heart rate following $MgSO_4$ administration to prevent hemodynamic fluctuations during intubation [13]. Our study also evaluated the cardiovascular effects of $MgSO_4$ and ketamine, revealing no significant differences in hemodynamic parameters between the two drugs. These findings suggest that both $MgSO_4$ and ketamine effectively manage postoperative shivering without compromising cardiovascular stability.

Postoperative body temperature monitoring was an essential parameter in our study. Tympanic temperature measurements in the recovery room indicated that all groups approached baseline values. The ketamine group exhibited lower body temperatures, reinforcing its potential role in thermoregulation. Both the $MgSO_4$ and ketamine groups had lower postoperative temperatures compared to the placebo group, suggesting a preventative effect on shivering.

Interestingly, shivering can occur even in normothermic patients [14]. While intraoperative hypothermia and postoperative vasoconstriction are key risk factors, non-thermoregulatory factors may also contribute [1]. Consistent with previous research, our study found no direct correlation between body temperature changes and postoperative shivering [6]. Tympanic temperatures in all groups gradually increased in the recovery room, indicating that shivering may not solely be temperature-dependent but influenced by other mechanisms.

$MgSO_4$ has been shown to lower the shivering threshold and exert central nervous system effects that aid in shivering control [15]. Dal et al. compared $MgSO_4$, pethidine, and saline in patients experiencing severe shivering and found that $MgSO_4$ and pethidine significantly reduced shivering compared to saline [15]. $MgSO_4$'s ability to mitigate shivering may be attributed to its neuromuscular effects and vasodilation. A meta-analysis by De Oliveira Filho et al. further highlighted that IV $MgSO_4$ not only reduced shivering but also decreased opioid consumption and postoperative pain intensity [16].

Ketamine's role as an NMDA receptor antagonist is crucial in managing both pain and shivering. Studies have demonstrated its efficacy in reducing postoperative shivering in both general and regional anesthesia settings [4]. Goich et al. recommended 0.5 mg/kg ketamine for shivering control after regional anesthesia due to its effectiveness and lack of significant cardiovascular side effects [18]. Our findings support these observations, showing that both $MgSO_4$ (30 mg/kg) and ketamine (0.5 mg/kg) administered as IV boluses at the end of surgery were superior to placebo in reducing shivering.

Postoperative shivering may stem from perioperative hypothermia due to anesthetic-induced thermoregulatory suppression. However, non-thermoregulatory factors, such as cutaneous vasodilation and pain, can also contribute [19]. Some hypothermic patients do not shiver, while postoperative pain has been shown to increase non-thermoregulatory tremors [20]. This highlights the importance of pain management in shivering treatment.

NMDA receptor antagonists help prevent central sensitization and hypersensitivity, making them valuable in acute pain management [21]. Liu et al. reported that ketamine and magnesium inhibit NMDA receptors non-competitively, with their combined effect being greater than their individual effects [22]. This may explain the enhanced impact of $MgSO_4$ and ketamine on both postoperative pain and shivering.

Magnesium also exerts analgesic effects by blocking calcium channels and NMDA receptors [23]. It can reduce opioid requirements and associated side effects [24]. A meta-analysis by Avci et al. showed that $MgSO_4$ administration in abdominal surgeries reduced both intraoperative and postoperative opioid consumption, reinforcing its role in postoperative pain management [25].

Limitation

This study has some limitations. First, since all participants were women, the generalizability of the findings to male patients is limited. Second, while tympanic membrane temperature measurement was chosen for its ease of use, factors such as earwax, airflow, or improper placement may affect accuracy. More reliable methods, like oesophageal or oropharyngeal measurements, could provide more precise results, particularly during surgery. Additionally, although some factors such as BMI and anesthesia duration were controlled, other potentially influencing factors like genetic differences and individual pain thresholds were not taken into account. The sample size of the study may be limited in detecting rare side effects. In the future, studies conducted with larger and more diverse samples may better evaluate the efficacy and safety of these treatment options.

Conclusion

In summary, MgSO4 and ketamine's effects on shivering and post-anesthesia recovery are in line with those of other research in the literature. Both medications in our trial decreased shivering in a comparable way and had safe side effect profiles. According to these results, ketamine and magnesium sulfate

are safe and effective treatments for tremors. It is also believed that these medications could be used more clinically to treat and manage postoperative shivering.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or compareable ethical standards.

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Conflict of Interest
The authors declare that there is no conflict of interest.

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